

Hypothesis: Septo-Optic Dysplasia Is a Vascular Disruption Sequence

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Septo-optic dysplasia, a variable combination of absence of the septum pellucidum, optic nerve hypoplasia, and pituitary abnormalities, makes little embryologic sense: components arise from different tissues and processes at different times, it is seen often with porencephaly, which is asymmetric, and rarely with other midline findings, genetic causes are exceptional, and occasional absence of the pituitary stalk is developmentally anomalous. Vascular vulnerabilities of components, anatomical overlap with findings of hydranencephaly and porencephaly, and a decreased maternal age effect similar to that of other abnormalities with presumed vascular origins, suggest a vascular disruption sequence instead, possibly involving the proximal trunk of the anterior cerebral artery. Am. J. Med. Genet. 69:235–236, 1997. © 1997 Wiley-Liss, Inc.

KEY WORDS: optic nerve hypoplasia; pituitary hypoplasia; septum pellucidum; vascular disruption sequence

INTRODUCTION

Septo-optic dysplasia (SOD) is a variable combination of absence of the septum pellucidum, optic nerve hypoplasia, and pituitary anomalies. Suggested pathogeneses, such as a sagittal midline dysplasia [Jones, 1988] or abnormal midline neuronal migration [Volpe, 1992], are wanting in several respects. A vascular disruptive sequence similar to porencephaly and hydranencephaly [Friede, 1989], possibly involving the proximal trunk of the anterior cerebral artery, is more likely.

PROBLEMS WITH SOD AS A DEVELOPMENTAL ANOMALY OR DYSPLASIA

1. There is no single time of development. The hypophysis forms by the seventh week, and the optic nerve soon after [O'Rahilly and Muller, 1992], while the septum pellucidum dates from 15–21 weeks [Bruyn, 1977].

2. Components arise from different tissues and developmental processes. The optic nerve arises from retinal ganglion cells, the anterior pituitary from oral ectoderm [O'Rahilly and Muller, 1992], and the septum pellucidum from the lamina terminalis, which forms from anterior neuropore closure and fusion of the lateral plates [Bruyn, 1977].

3. SOD is often seen with porencephaly [Barkovich et al., 1989; Barkovich and Norman, 1989; Kuban et al., 1989; Menezes et al., 1988], which is typically asymmetric, and difficult to explain as a midline problem.

4. Full SOD is rare in anomalies of related embryonic structures. Developmental absence of the septum pellucidum involves a process that can encompass the corpus callosum [Sarwar, 1989], which is rarely seen with SOD. Also, mild forms of holoprosencephaly, a true midline anomaly with pituitary anomalies and an absent septum, generally show optic colobomas instead of optic nerve hypoplasia [Cohen, 1989].

5. Pituitary stalk hypoplasia (or absence), an occasional finding in SOD [Kaufman et al., 1989], makes no embryologic sense, since the stalk is the site of outgrowth of this organ [O'Rahilly and Muller, 1992].

6. True dysplasias involve tissue properties, and are typically genetic, as with ectodermal dysplasias [Freire-Mala and Pinheiro, 1984], for example. Yet SOD is almost always sporadic.

7. Opitz has noted that developmental field defects should be causally nonspecific [Freire-Maia and Pinheiro, 1984]. However, SOD is exceptional in syndromes, suggesting a specificity of origin atypical for this sort of developmental process.

SUPPORT FOR A VASCULAR DISRUPTIVE ORIGIN

1. All components are vulnerable to vascular events:
a) The septum pellucidum is susceptible to atrophy or destruction with pressure or stretching [Friede, 1989].

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Received 14 February 1995; Accepted 6 August 1995

b) Embryologically, the optic nerve is surrounded and penetrated by a primitive vascular plexus, and the chiasmatic plexus anastomoses with the infundibular vascular system [Duke-Elder and Cook, 1963]. c) The pituitary is highly vascular, and liable to infarction under several circumstances [Vance, 1994], with suggestions of a particular neonatal vulnerability of the infundibulum [Kelly et al., 1988].

2. Optic findings with SOD and hydranencephaly [Herman et al., 1988], a vascular sequence [Friede, 1989], can be similar. A possible association of optic nerve hypoplasia and prenatal vascular encephalopathies has also been proposed [Burke et al., 1991].

3. SOD often occurs together with porencephaly (see above), which is considered a vascular disruption [Friede, 1989].

4. Septo-optic dysplasia associates significantly with decreased maternal age [Lippe et al., 1979]. This also occurs with other presumed prenatal vascular disruptions, such as gastroschisis [Torfs et al., 1994] and hydranencephaly [Lubinsky et al., 1997].

ANATOMIC CORRELATION

The proximal trunk of the anterior cerebral artery (the segment prior to origin of the anterior communicating artery) passes over the optic tract and chiasm. It gives rise to an inferior group of arteries that supply the superior surface of the optic nerves and chiasm, and to a superior group that goes to the anterior hypothalamus, the septum pellucidum, and other structures. These relationships make this vessel a candidate for involvement in the pathogenesis of SOD; anatomic variations [Crosby et al., 1962] may be predisposing factors.

CONCLUSIONS

Septo-optic "dysplasia" makes more sense as a vascular disruption sequence, similar to porencephaly and hydranencephaly, than as a primary developmental anomaly. Events involving the proximal trunk of the anterior cerebral artery are most likely to be pathogenetically involved.

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